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HAEMATOBLASTS AND BLOOD PLATELETS.

DR. M. L. HOLBROOK, of New York.

Although many studies and publications have been made during the last twenty years on the morphological elements of the blood, we have not yet reached an understanding of the significance of certain form-elements, known as the "Third Corpuscles."

In my studies of human blood, extending over several years, I have reached certain conclusions which I wish to bring before this society.

The reason why so much discrepancy of opinions on certain points prevails among observers is two fold: first, the structure of the red blood corpuscles is not agreed upon by the majority of microscopists, and second, under the term, the "third element," both Haematoblasts and blood platelets have been included by most authors who have written on the subject.

During the last two years I have laid before you observations, which I think go far to prove the correctness of Elsberg's assertion made in 1879, that the structure of the red blood corpuscle is reticular, the same as that of the colorless blood corpuscle, the difference being, that in the former the meshes of the reticulum are filled with a chemically complicated substance, generally termed "haemoglobin"; whereas, in the latter, the meshes hold a colorless nitrogenous liquid, the "paraplasma" of French microscopists. It seems to me that no understanding of the so-called "third element" is possible, unless we admit the reticular structure of the red blood corpuscles. As to the second point, it will be the topic of the present paper. I will state in advance, that the haematoblasts, and the blood platelets, are not identical formations, but of widely different origin and significance.

As to the method of investigation I wish to emphasize, as I have done in previous years, that reliable observations are possible, only when we take the blood directly from the blood vessels and immediately transfer it to a moist chamber and under the microscope. I need not again describe how to prepare specimens, but I will add, that I lay emphasis upon the size of the droplet of blood to be taken, as well as the rapidity of transferring it to the slide. The size of the droplet should be at least as large as a medium sized pin's head. Such an one will spread uniformly under a three quarter inch cover glass whose margins have beforehand been oiled. Smaller drops do not spread so evenly, and the thin places are apt to dry up under the influence of the air inclosed under the cover.

No time should be wasted in squeezing out a droplet too small from too slight a wound with the needle. A few seconds delay will suffice to cause crenation of the majority of red blood corpuscles, even though in summer heat, whereas the contour will be almost uniformly smooth, if there is no delay in removing the blood into the moist chamber of the slide.

I object to the addition of any reagent, such as a solution of osmic acid, Pacini's preserving liquid, or even a solution of table salt : they all quickly alter the appearance of the blood, and lead to misconceptions.

Nothing but the serum of the blood should be allowed to bathe the blood corpuscles. In it—as I have shown in a previous paper—they may be preserved for several days.

I. HAEMATOBLASTS.

Haematoblasts are shining or lustrous, homogenous globules or disks, of a marked, yellow color, measuring 1.5 and 3.5 micromillimeters in diameter, up to nearly the size of fully developed red blood corpuscles. They are juvenile forms of the red corpuscles present in large numbers in the blood of the newly born, and in small numbers in the blood of healthy adults. I have seen them in small numbers in the blood of a healthy man sixty-three years of age. They are invariably augmented in number whenever there has occurred a considerable hemorrhage, or after frequent slight hemorrhages. We see them with great regularity in urine holding red blood corpuscles to a varying number, due to hemorrhages induced by tumors of the bladder, especially benign papilloma, or hemorrhages from the pelvis of the kidneys, due to so-called renal calculi. Their number varies according to the severity and frequency of the hemorrhages. They have nothing to do with wasting diseases, such as tuberculosis, cancer, syphilis, etc. etc. Neither are they augmented in numbers in chlorosis.

This I think goes far to prove, that haematoblasts are juvenile forms of red blood corpuscles, and their most characteristic feature is their yellowish color, due to the presence of haemoglobin, even in the earliest recognizable stages, when they do not exceed in size a granule. I have stated before, that haematoblasts are homogeneous and apparently structureless. This is true only of the smallest forms; as soon as they have reached the size of about 3 micromillimeters under a magnifying power of 1,000, to 1,200 diameters, we recognize in them an extremely narrow and faint reticular structure, especially after their exposure to a solution of $\frac{1}{5}$ of 1 per cent. of chromic acid, or a 40 to 50 per cent. saturated solution of bichromate of potash. The latter brings forth distinctly the reticular structure of fully developed red blood corpuscles.

The smallest haematoblasts under the influence of these solutions are either unchanged, or exhibit a small central or eccentric vacuole, whereby they are rendered ring-shaped.

Haematoblasts up to half the diameter of a red blood corpuscle resist, at least for some time, a solution of glacial acetic acid with equal parts of water. They retain both a yellow tint and a smooth contour, whereas fully developed red blood corpuscles by this reagent are either rendered flat, much enlarged, crenated into many shapes, or broken up as will be described later.

The smallest haematoblasts always retain a smooth surface, even though the red blood corpuscles in the same specimen have become crenated all over. When the haematoblasts have reached about half the size of fully developed red blood corpuscles, they assume a finely crenated surface, the crenations appearing like extremely delicate, almost invisible needle-shaped projections from their margins, and not blunt, or knob-like, as are those of fully developed red blood corpuscles.

As to their origin I shall not make positive statements for the present. I am sure, however, that the formerly received opinion as to the origin of red blood corpuscles from the colorless blood corpuscles is erroneous.

Haematoblasts are formed in the tissues of the embryo or the foetus, whenever one type of connective tissue changes into another: for example, cartilage into bone. Haematoblasts are formed, whenever in the process of development of the tissues, new blood vessels arise. They are formed in the adult in all lymph-structures, mainly in the lymph ganglia, and in the spleen, throughout life. The older a person grows, the less of lymphatic structures are present in the organism, hence haematoblasts are found only in small numbers in the blood of very aged people.

Final statements as to the origin of haematoblasts I will postpone until I have finished some studies of the *area vasculosa* of the embryo of the chicken.

Haematoblasts are granules or isolated lumps of living matter not yet of the size of a red blood corpuscle. They are early forms of red blood corpuscles and develope into such. They are homogeneous if small, the size of granules, say 1.5 micromillimeters in diameter, and, of a more distinctly reticular structure, the nearer they reach the size of the red blood corpuscles. They are from the very beginning saturated with haemoglobin.

Most writers quote Hayem as the discoverer of these bodies. This is erroneous, for neither the name "haematoblast," nor an accurate description thereof can be credited to him. Foster's Medical Dictionary is, so far as I know, the only work mentioning C. Heitzmann as the originator of the name. (See Art. "Haematoblast," in that work.) Foster defines haematoblasts correctly when he says they are miniature red blood corpuscles. This term is applied to small colorless, circular or ovid bodies, ½ to $\frac{1}{6}$ the size of red blood corpuscles, circulating in the blood of mammals. It is, according to Foster, probably identical with the haematoblast of Hayem, and the blood-plate of Osler. This is an error, the same one Hayem himself made when describing the haematoblast in 1877.

Heitzmann, (Studien am Knocken und Knorpel; "Medicinische Jahrbucher", 1872,) described the changes occurring in the hyaline cartilage, preceding the formation of bone tissue. At the border of the hyaline cartilage he found isolated lumps of living matter of high refraction, of a yellowish color, evidently arising from cartilage corpuscles. He says: "As the shining solid corpuscles exhibited stages of development, advancing to the formation of nearly perfect red blood corpuscles, I considered them to be juvenile forms of the latter, and proposed for their designation the term haematoblast. I concluded, that a part of the cartilage corpuscle, or a portion of the body of such corpuscle, had become transformed into haematoblasts."

His statements are illustrated, and have been corroborated by Kassowitz and others. In 1873 another paper appeared by this author, in which the new formation of blood vessels is described in the process of transformation of cartilaginous into bone tissue, likewise with numerous illustrations, in which the haematoblasts are seen lying in vacuoles of elongated formations of living matter in the future blood vessels. He claims that both blood corpuscles and blood vessels originate simultaneously, the former from isolated lumps of living matter which he termed haematoblasts, the latter from elongated tracts of living matter hollowed out by vacuolation, and the accumulation of a liquid, in which the haematoblasts are suspended. From this it is evident, that Heitzmann was the discoverer of the haematoblasts, the first to correctly describe them, and the first to give them a name.

In 1877, G. Hayem presented to the Academy of Sciences, Paris, in succession, with only brief intervals of time, four papers published in the Comptes Rendues, vol. 84, which relate to the red blood corpuscles. In the first paper he speaks of the anatomical features of the blood of the newly born. He states that the sizes of the corpuscles are more varied than in the blood of the adult. In the second paper he discusses the nature and significance of the small blood corpuscles. He contradicts a prevalent opinion that these corpuscles indicate a retrograde change, or atrophy; on the contrary he concludes, from the number of facts which he has observed in convalescent persons after acute wasting diseases, in anaemia, in menstruation, etc., that these small elements which he terms dwarfed corpuscles are young red blood corpuscles incompletely developed.

In the third paper, upon the development of the red blood corpuscles of the blood of oviparous vertebrates, he says: "The blood of oviparous vertebrates constantly holds colorless cells differing essentially from white blood corpuscles. These elements in progressive development become perfect red blood corpuscles, and for this reason he proposes to call them by the name of "Haematoblasts."

In the fourth paper upon the development of the red corpuscles in the blood of the higher animals, *i. e.*, viviparous vertebrates, he states that the haematoblasts in the blood of men and viviparous vertebrates are very small, delicate, slightly refracting elements of a contour almost invisible, with a diameter of 1.5 to 3 micromillimeters. Immediately after the removal of the blood from the blood vessels the haematoblasts become thorny and are apt to form groups or clusters, which latter feature is less pronounced in the blood of man than in certain animals. They play an important part in the formation of fibrin.

In his conclusion he states, that the red blood corpuscles arise from more or less regular small elements which are colorless, delicate, and quickly changed, or modified as soon as removed from the blood vessels of living creatures. From the description of Hayem it plainly follows that he designated as haematoblasts two form elements which I hope to show are entirely distinct.

II. BLOOD PLATELETS.

The first to see in fresh blood granules, granular masses or plaques, was Max Schultze. [Archiv fur Mikroscopische Anatomie Vol. 1, p. 38, 1861.] Instead of the word plaque, I adopt the name platelet, it being the diminutive for plate, and identical with the French plaque.

Blood platelets are colorless lumps of living matter varying in size from those just visible up to the size of about ½ the diameter of a red blood corpuscle.

The smallest granules as seen under good immersion lenses are apparently homogeneous or structureless. The larger the granules are, the more we are able to see in them an extremely delicate, faintly pronounced reticular structure. When small they present a peculiar greenish, shining appearance, characteristic of all granules of living matter.

They lack the yellowish tint seen in the haematoblasts. Small granules are nearly uniform in their diameter, are often slightly angular, *i. e.*, provided with from two to four conical projections.

The more these granules swell, owing to their taking in of liquid from the surrounding plasma of blood, the more they assume a grayish color, a discoid shape, a smooth contour, and a faint reticular structure.

The easiest way to produce platelets is to treat the blood corpuscles with glacial acetic acid, diluted with equal parts of water.

For this purpose a droplet of the solution of the acid is placed upon the skin, preferably of the palmar surface of the thumb of the left hand. It is pricked directly through this droplet. Both the blood secured, and the acetic acid are at once transferred to the slide and quickly covered with a thin cover glass, always of course oiled as already described. In my own blood, platelets are extremely scanty. As soon, however, as acetic acid is mixed with it, hundreds of them appear of all sizes from the minutest granules, up to the half size of a red blood corpuscle, the smallest being slightly angular, glossy and of a greenish refraction ; the larger pale gray, smooth. discoid, and faintly reticulated.

Influenced by the preparation of acetic acid the red blood corpuscles will in a few minutes become enlarged to nearly three times their original size, much flattened and deprived of coloring matter.

The experiment I have here described was first made by Norris of England. (See under word "Haematoblast," Foster's Medical Dictionary) who thought he had thus discovered a new element in the blood, and proposed for it the awkward name, "Invisible corpuscles of the blood." He evidently did not take into account the fact that the platelets were artificial products caused by the breaking up of the blood corpuscles under the influence of acetic acid. Norris's experiment is valuable, however, inasmuch as it shows us how to produce them in large numbers in a short time.

The question now arises, what are the platelets? I may state that without doubt they are products of the red blood corpuscles caused by their disintegration into fragments of varying sizes.

My reasons for this statement are the following :

1. In specimens of fresh blood transferred at once to the microscope I have occasionally seen, when the red blood corpuscles were distinctly crenated, knobs hanging upon the corpuscles by means of a slender pedicle. These knobs after the pedicle breaks,

float away freely in the surrounding serum, exhibiting slightly angular contours and all the features of blood platelets.

2. If the blood of persons of an impaired constitution is prepared and kept for a few days, being examined daily, we shall, beginning perhaps on the 2nd or 3d day notice clusters of platelets which judging from their arrangement must have arisen from disintegration of the red blood corpuscles.

3. If we treat fresh blood with glacial acetic acid, diluted with equal parts of water, the red blood corpuscles are immediately transformed into large flat and pale plates, as already described, studded with blood platelets varying in size from the minutest visible granule, up to those of ordinary size. At the same time numerous platelets have appeared in the surrounding blood plasma.

4. The observation that platelets arise from red blood corpuscles had been made previously by L. Elsberg, by treating these bodies with 40 to 50 per cent. solution of bichromate of potash. (Annals of the New York Academy of Science, Vol. I, 1879.)

He says, "An indentation at the periphery of the red blood corpuscles is due to locally limited contraction of the network in the interior of the corpuscles. Contractions of the living matter in one part of the periphery will bring about a protrusion of a flap at another, the flap being bounded by the other layer of the corpuscle. Segmental contractions of the network will produce a rupture of the outer layer of the corpuscle, with projection of a pediculated granule or knob, formerly a part of the interior network; continued contraction will be followed by rupture of the pedicle and the production of either the so called detritus, or small granules, or when the protruded knob is larger, or has become swelled, of a pale grayish disk."

Elsberg also adds the following statement: "The peculiar corpuscle believed to be characteristic of syphilis by Lostorfer, and proved by Stricker to be present in the blood of individuals broken down by that and various other diseases, are nothing but such disks, *i. e.*, portions of the colored blood corpuscles protruded from the interior, detached and more or less swelled. As persons in low states of health have a relatively small amount of living matter in the same bulk, or in other words, only a delicate network within a protoplasmic body, or plastid, the so-called cell, such a network suspended in a relatively large amount of fluid, can much more easily contract and cause a rupture of the outer layer, than in the case of healthy persons, within whose plastids there is relatively less room for contraction to take place."

All the named observations explain why a platelet has no color and holds no haemoglobin. If we recall the fact that a red blood corpuscle is made up of a reticulum of colorless matter, in whose meshes is suspended more or less haemoglobin, we readily understand that the platelets, being exclusively formations of living matter, lack haemoglobin altogether. While I am positive that the platelets are products of the disintegration of red blood corpuscles, I have made numerous observations which show that they also originate from granules, or rather points of intersection of the reticulum of colorless blood corpuscles. From whatever source, they are under all circumstances identical with granules of living matter.

As to the significance of the blood platelets, I do not claim that they are pathological. This much however, is certain, that in the blood of perfectly healthy persons they are either very few or entirely absent. On the contrary, the more a person's health is impaired by chronic disease, the more certain we are to find a considerable number of them in the blood, when taken from the vessels a few seconds before microscopical examination. In persons suffering from Syphilis, from Cancer, from Tuberculosis, or even from Neurasthenia, we find them in considerable numbers. Lostorfer, (Medicinische Jahrbucher, 1871), was, as he frankly admitted, mistaken in bringing the platelets into special relation with Syphilis.

R. L. Watkins, (The Medical Brief, Vol. 21, 1893) is, also mistaken in bringing the platelets into exclusive relation to Tuberculosis, for these bodies are always present in just as large numbers in the blood of persons suffering from other chronic wasting diseases.

Wm. Osler in his Cartwright lectures 1886, claims that the third corpuscle is identical with the haematoblast, as most other observers do. He quotes Hayem as the discoverer of the haematoblast as well as of the blood platelet. I have drawn attention to the fact in the first part of my paper, that Hayem is not the discoverer of the haematoblast, and now I will also add that Hayem was in error in confounding the haematoblast with the blood platelet.

Osler's views are marred by the acceptance of Hayem's error. There can be no doubt that Lostorfer in 1871, first saw the platelets, although he misinterpreted their significance. We may call Max Schultz, the discoverer of the granular masses in the blood, though this excellent observer had in 1860 no idea of the life and the structure of the red blood corpuscles which he merely considered as chemical constituents of the blood.

Guilio Bizzozero, (Archiv. Ital. de biol. 1882), states, that the platelets, which he terms plaques, serve as centers of coagulation of the fibrin, and play an important part in the formation of the white or fibrous clot of the thrombus, obliterating the calibre of the injured blood vessels, forming masses that constitute the chief element in the white of fibrous thrombus.

Wm. Osler was first to observe in 1861, that in the more superficial part of white thrombi, the blood platelets were present.

Many observations have proved that both haematoblasts and blood platelets circulate in the vascular system of living animals.

If we consider the fact that healthy persons have, in their red blood corpuscles a compact reticulum of living matter, whose meshes are filled with haemoglobin, while debilitated persons, on the contrary have a delicate reticulum in their red blood corpuscles and comparatively little haemoglobin, probably also of less consistency than in vigorous persons, we are at once in the position to understand the origin and the significance of platelets.

The living matter during the life of the organism is at no time in perfect rest. Perfect rest means death. Contraction of the living matter in the red blood corpuscle of a healthy person will have but little effect, and will rarely cause the protrusion and detachment of platelets. The more delicate the reticulum, the more effective will be the result if its contractions, especially if the haemoglobin is scarce and of a more liquid consistency. Contractions of living matter in this instance will easily produce knob-like protrusions on the periphery of the red blood corpuscle, which, being detached, will appear in the shape of platelets floating in the serum of the blood.

In my opinion the presence of platelets in the blood in large numbers is not a pathological feature as such, but merely an indication of a pathological state of the system. Every chronic disease that causes a wasting of living matter, and a decrease in the amount of haemoglobin, will cause the appearance of platelets in varying numbers within the vascular system.